

# **QALSODY®**

## **Category:**

Best Product for Orphan/Rare Diseases

## **Company Name:**

Biogen

## **Product/Solution Name:**

QALSODY® (tofersen)

## **Compound/Tech Name:**

Tofersen

## **Trade Name:**

QALSODY

## **Corporate Name:**

QALSODY

## **Date of Approval:**

2023-04-25

## **Indications:**

For the treatment of adults with amyotrophic lateral sclerosis (ALS), associated with a mutation in the superoxide dismutase 1 (SOD1) gene.

## **Therapeutic Areas:**

Superoxide dismutase 1 (SOD1)-amyotrophic lateral sclerosis (ALS)

## **General Information File Document upload:**

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## **Background information and need for drug / device:**

Amyotrophic lateral sclerosis (ALS) is a rare, progressive, and uniformly fatal neurodegenerative disease resulting in the loss of motor neurons in the brain and the spinal cord responsible for controlling voluntary muscle movement. People with ALS experience muscle weakness and atrophy, causing them to lose independence as they steadily lose the ability to complete activities of daily living. As the disease progresses and the brain loses connection with the muscles, patients lose their ability to move, speak, eat, and breathe. The average life expectancy for people with ALS is three to five years from time of symptom onset, underscoring the limitations of treatment options that were available prior to QALSODY.

More than 15 percent of people with ALS are thought to have a genetic form of the disease. Multiple genes have been implicated in ALS, including SOD1. SOD1-ALS is a rare form ALS that is diagnosed in approximately 2 percent of all ALS cases, with about 350 people in the United States living with the disease.

## **Background File Document upload:**

N/A

## **History of the development of the solution/product:**

Dr. Robert H. Brown, an internationally known researcher and physician, discovered SOD1 (Superoxide dismutase 1) as the first gene linked to ALS in 1993. Ten years later in 2003, Drs. Don Cleveland, Richard Smith, and Timothy Miller worked with Ionis Pharmaceuticals to develop an antisense oligonucleotide (ASO) targeting SOD1. Biogen collaborated with Ionis on the development of tofersen, leading to encouraging data from the Phase 1/2 study that were published in 2019 in the New England Journal of Medicine. The data showed that tofersen reduced levels of cerebrospinal fluid SOD1 concentrations and resulted in improvements in function, breathing and strength – demonstrating that the treatment accomplished what it was designed to do biologically and clinically, supporting the initiation of the Phase 3 VALOR study. The 2021 VALOR topline results did not show a statistically significant benefit with tofersen over placebo – however trends across multiple endpoints suggested tofersen benefitted patients. What wasn't clear at the time was why.

In the coming months, Biogen conducted in-depth reviews of the data and conducted a number of statistical analyses. In a first for the ALS field, the Biogen team used neurofilament, a biomarker of neurodegeneration, to account for the extreme disease heterogeneity that exists in ALS. With the benefit of an additional six months of data and neurofilament as a marker of disease progression rate at baseline, additional data were presented in 2022 that showed treatment with tofersen led to benefits in measures of survival, respiratory function and hand strength.

Biogen began conversations with regulators and by the end of 2022 had submitted new drug applications in the US and EU. The FDA approval of tofersen, under the accelerated approval pathway, in 2023 based on reductions of neurofilament demonstrated the enormous importance of having a biomarker in ALS. For a disease area that has been plagued with failures over decades, the changes patients saw with tofersen treatment and the use of neurofilament provided the field with hope that with the right tools, ALS drug development could be successful. This was recently followed by the EU approval of QALSODY – which had not approved a new medicine for ALS in 25 years.

Over the last year, people receiving QALSODY have spoken to reporters about their experiences. Jessica Morris recently shared her story with reporters in a local TV interview and with USA Today. She comes from a family plagued by SOD1-ALS (22 of her relatives had the same form of the disease). She expected to only be able to plan for the short-term, including a family vacation, given the progressive and deadly nature of the disease, however, she is now thinking towards her future.

Biogen has not finished studying how QALSODY can help people living with SOD1-ALS in the ATLAS study which is designed to determine whether QALSODY can delay clinical onset of ALS when given to people with a SOD1 genetic mutation, before they show symptoms. The results from this study will act as the confirmatory study for the FDA, a requirement of the accelerated approval to verify clinical benefit, and will support FDA traditional approval and regulatory submissions around the world.

## **Development File Document upload:**

N/A

## **Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:**

Tofersen means that people with SOD1-ALS will have a treatment option at the time of their diagnosis. Prior to tofersen, slowing or stopping disease progression was unheard of. From a clinical and community standpoint, the reduction in neurofilament seen with tofersen shows for the first time that it is possible to address the biological cause of ALS. Timothy Miller, M.D., Ph.D, ALS Center Director at Washington University School of Medicine, St. Louis, states: “More than 25% of people taking tofersen have shown sustained improvements. This is unheard of among people living with ALS and has been incredible to witness as an ALS physician. This is not only tremendously impactful for those with the genetic subset of ALS treated by tofersen, but teaches the whole ALS field that the right drug can have a significant impact on the clinical course.”

Historically, new drug development in ALS has been focused on people living with the disease, with no expectation that damage done by the disease could be limited prior to the onset of symptoms. The ATLAS trial has the potential to show that tofersen could delay the onset of symptoms. While tofersen treatment may directly change the lives of a small percentage of people with ALS, it represents a future of ALS treatments targeting the cause of the disease and an industry that is devoted to delaying if not completing stopping the disease. The learnings from tofersen have led to evolution of ALS trial design and dictate the requirement for stronger biological plausibility of therapeutic targeting, thereby accelerating the translation of discoveries into human impact.

Additionally, with QALSODY, Biogen has advanced the role of neurofilament in the development of new medicines for ALS and other neurodegenerative diseases, with the potential to accelerate further discovery in the field. Precious research dollars in these diseases can be used more effectively to advance drugs that are proven to reduce neuronal damage as measured by neurofilament. Most importantly, QALSODY serves as a beacon of hope for everyone with ALS by telling the patient community that research and science are working, and that this disease can be treated.

### **Innovation File Document upload:**

N/A

### **Please provide appropriate references (PubMed, Abstract, Website):**

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